To Jan

Access DB# 92993

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Brian Kwon Examiner #: 7845 Date: 5/1/03
Art Unit: 1614 Phone Number 308-5379 Serial Number: 10/061510
Mail Box and Bldg/Room Location: CM1 1004 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEJ

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Clear micellized formula of beta-carotene

Inventors (please provide full names): Wenjie Li

Earliest Priority Filing Date: 2/2002

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

RECEIVED MAY - 1 2003 GROUP 1600

See attached

tx for oral leukoplakia (claim 1)
with composition i) acids; ii) polyol iii) fatty acid
ester iv) surfactant v) β-carotene

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Jan	NA Sequence (#)	STN
Searcher Phone #: 4458	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 5/6/03	Bibliographic ✓	Dr.Link
Date Completed: 5/6/03	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 15	Patent Family	WWW/Internet
Online Time: 70	Other	Other (specify)

PTO-1590 (8-01)

ORAL LEUKOPLAKIA

Synonym: idiopatic leukokeratosis

As a clinical entity, **oral leukoplakia** has been defined as a whitish patch or plaque which cannot readily be characterized as any other lesion or disease. The term is **not applicable** as long as the lesion can be directly associated with any chronic - physical or chemical - irritant; *except for the use of tobacco.* The term would, in a very strict sense, eventually not be applicable in for instance cases of hairy **leukoplakia** in AIDS patients and *polykeratosis of Touraine.*

Oral leukoplakias are more often seen among heavy users of tobacco and alcohol; the term also being applied to lesions associated with snuff dipping, betel nut and tobacco chewing, and reversed smoking. The frequency with which oral leukoplakias are seen among alcoholics have often been related to concommitant nutritional, and then especially vitamin, deficiencies. Other contributory factors are actinic radiation, intraoral electrogalvanic phenomena and xerostomia.

The prevalence of **leukoplakia** is about 3%. The typical patient is an elderly man, and the lesion is most commonly seen in the buccal mucosa. It is least likely to occur on the tongue and in the floor of the mouth. The clinical lesions have been divided into the following groups:

- homogeneous **leukoplakia** (**leukoplakia** simplex) (I1)
- non-homogeneous **leukoplakia**
    - nodular **leukoplakia**
    - speckled **leukoplakia**
    - erythroleukoplakia
- verrucous **leukoplakia** (verrucous hyperplasia, oral florid papillomatosis)

Leukoplakias are essentially without symptoms, but the non-homogeneous types may cause a burning pain, especially when eating heavily spiced food.

The **histological picture** of oral leukoplakias reveals a spectrum of changes, ranging from the presence of a normal hyperothokeratinized epithelium (75-80%) to the presence of features characteristic of anaplastic squamous carcinomas (20-25%). In between these extremes, and with particular reference to the findings that around 4-6 percent of oral leukoplakias eventually turn malignant; i.e. later reveal the presence of an oral carcinom, clinicians should be particularly aware of - attach a particular significance to - any mentioning of the histopathological presence of **epithelial atypia**.

Adapted, with kind permission, by BKGS.

(originally from an early version of ORAMED©HM 1990 to an early version of INFODONT)

REFERENCES: AUTHOR(S) | TEXTBOOK | REFBASE | IMGBASE

1: Oral Oncol. 1997 Jul;33(4):231-6. Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Chemoprevention of oral leukoplakia with vitamin A and beta carotene: an assessment.

Sankaranarayanan R, Mathew B, Varghese C, Sudhakaran PR, Menon V, Jayadeep A, Nair MK, Mathews C, Mahalingam TR, Balaram P, Nair PP.

Unit of Descriptive Epidemiology, International Agency for Research on Cancer, Lyon, France.

We conducted a double-blind placebo-controlled trial to evaluate the chemopreventive potential of either vitamin A alone or beta carotene alone in subjects with oral leukoplakia in Kerala, India. We randomised 160 fishermen and women with oral precancerous lesions to receive oral vitamin A (retinyl acetate 300,000 IU/week x 12 months, n = 50), or beta carotene (360 mg/week x 12 months, n = 55), or placebo (n = 55). Blood, saliva and urine samples were collected at baseline and at exit to study serum micronutrients and mutagenicity assays. Biopsies of the mucosal lesions at entry were performed for histopathological exclusion of malignancy. The subjects were examined once every 2 months to establish clinical response of lesions and toxicity, if any. The results are based on 43 complaint subjects on placebo, 42 on vitamin A and 46 on beta carotene. The complete regression rates were: 10% in the placebo arm, 52% with vitamin A and 33% with beta carotene ($P < 0.0001$). Homogeneous leukoplakias and smaller lesions responded better than non-homogeneous and larger lesions. No major toxicities were observed. Half of the responders with beta carotene and two thirds with vitamin A relapsed after stopping supplementation. Serum beta carotene concentration increased substantially with beta carotene administration while with vitamin A supplementation there was no change in serum retinol levels. In the vitamin A treated group there was a significant decrease in serum alpha tocopherol. Vitamin A administration resulted in a significant remission of oral leukoplakia without any side effects of prolonged vitamin A supplementation. The results of this study, as well as those from previous studies, appear to provide strong supporting evidence to justify long term trials with vitamin A in subjects with high-risk leukoplakias with oral cancer as an endpoint.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 9307711 [PubMed - indexed for MEDLINE]

1: Oncology. 1992;49(2):77-81. Related Articles, Links

Entrez PubMed

PubMed Services

Related Resources

Treatment of oral leukoplakia with beta-carotene.

Toma S, Benso S, Albanese E, Palumbo R, Cantoni E, Nicolo G, Mangiante P.

Istituto Nazionale per la Ricerca sul Cancro, Genova, Italia.

Over the past few years, beta-carotene has progressively gained ground as a drug chosen in the treatment of oral leukoplakias, thus making it possible to reduce the use of 13-cis-retinoic acid, which was shown by many studies to be highly toxic while beta-carotene has proved to have no significant side effects and hence to be much more suitable in oral premalignancy. In 1989, a phase II study of patients showing oral leukoplakias and treated with beta-carotene (90 mg/day) was begun. A total of 23 patients (aged between 17 and 85) were included in the study and 18 (8 male and 10 female) were evaluated. Eight patients (44.4%) had objective responses (6 complete, 2 partial). Four CR and a PR appeared unexpectedly within 2-7 months after the end of the therapy. The lesions were macroscopically and histologically examined at entry; in the evaluated patients, two types of alterations were found: atypical hyperplasia (16 patients) and dysplasia (2 patients). No signs of significant toxicity were detected; only in 1 patient treatment had to be interrupted for 1 week. The results of this study show the fair efficacy of beta-carotene against oral leukoplakias, but further confirmations through controlled clinical studies are needed.

Publication Types:
- Clinical Trial

PMID: 1574255 [PubMed - indexed for MEDLINE]

Go Back | Nutrition for a Living Planet - Home Page

Beta Carotene - Vitamin A

Vitamins are compounds that you must have for growth and health. They are needed in small amounts only and are usually available in the foods that you eat. **Beta-carotene** is converted in the body to vitamin A, which is necessary for healthy eyes and skin.

Beta carotene, which is found in plants, is a precursor of vitamin A. The body converts **beta carotene** to vitamin A. It occurs mainly in fruits and vegetables that are deep yellow, orange, or dark green in color, such as carrots, squash, yams, peaches, apricots, spinach, collard or mustard greens, and broccoli. It is an antioxidant, a compound that may prevent cancer-causing substances from damaging DNA. Epidemiologic studies have linked high intake of foods rich in **beta carotene** and high serum levels of the micronutrient to a reduced risk of cancer, particularly lung cancer. Ordinary cooking does not destroy **beta-carotene**.

A lack of vitamin A may cause a rare condition called night blindness (problems seeing in the dark). It may also cause dry eyes, eye infections, skin problems, and slowed growth. Your health care professional may treat these problems by prescribing either **beta-carotene**, which your body can change into vitamin A, or vitamin A for you.

Some conditions may increase your need for vitamin A. These include:

- Cystic fibrosis
- Diarrhea, continuing
- Illness, long-term
- Injury, serious
- Liver disease
- Malabsorption problems
- Pancreas disease

Claims that **beta-carotene** is effective as a sunscreen have not been proven. Although **beta-carotene** supplements are being studied for their ability to reduce the risk of certain types of cancer and possibly heart disease, there is not enough information to show that this is effective.

Beta-carotene may be used to treat other conditions as determined by your doctor.

It is well documented that people who consume diets high in fruits and vegetables have a reduced risk of heart disease and certain cancers. Fruits and vegetables are rich in **beta-carotene** and other nutrients that

may be beneficial.

Vitamins alone will not take the place of a good diet and will not provide energy. Your body needs other substances found in food, such as protein, minerals, carbohydrates, and fat. Vitamins themselves often cannot work without the presence of other foods. For example, some fat is needed so that **beta-carotene** can be absorbed into the body.

Daily servings of dark green and deep yellow vegetables and tomatoes boost immune response, a preliminary study suggests. If the findings hold up in further research, eating more vegetables rich in **beta carotene** and related carotenoids--lutein and lycopene--may help people ward off a cold or flu as well as protect against cancer.

After three weeks, the volunteers had a 33 percent increase in immune response as measured by the ability of their T cells to multiply. This is a good measure of immune system function because T cells play a vital role in the immune response to foreign organisms and cancer cells.

As potent antioxidants, these carotenoids are thought to contribute to the lower rates of heart disease, cancer and other diseases of aging among populations that eat a lot of fruits and vegetables.

Reported in the Proceedings of the UJNR Protein Resources Panel, 25th Annual Meeting, 1996, the findings suggest that carotenoid-rich vegetables also stimulate the immune system.

Researchers also found more evidence suggesting carotenes act as antioxidants to protect the body from harmful oxidation that could contribute to heart attack, stroke and cancer. During the low-carotene stints, researchers recorded several biochemical signs of oxidative damage. For example, they found more carbonyl compounds--breakdown products of oxidation--in the volunteers' blood and breath.

Older people who get plenty of **beta carotene** may have a better chance of preventing virus infections or a cancerous growth. A wealth of epidemiological evidence has linked a high intake of green leafy and deep yellow vegetables--both rich in **beta carotene**--with lower rates of many types of cancer.

Men over age 65 who took a 50-milligram **beta carotene** supplement every other day during the 12-year-long study had natural killer cells that were more active than those in their counterparts who got a placebo. Natural killer cells--or NK cells--are the immune system's sentinels, ever on watch for viruses and cancer cells. They recognize an enemy immediately and destroy it, using proteins to punch holes in its outer membrane. This activity is thought to be an important component of cancer prevention. So ARS researchers tested NK cell activity in 59 men in the physicians study.

The **beta carotene** dosage used in the physicians study is equivalent to eating two regular-size carrots or one and one-half sweet potatoes daily.

Beta-Carotene has been reported to produce regressions in patients with oral **leukoplakia**, a premalignant lesion. In this multicenter, double-blind, placebo-controlled trial, subjects were given **beta-carotene**, 60 mg/d, for 6 months. At 6 months, responders were randomized to continue **beta-carotene** or placebo therapy for 12 additional months. Nutritional intake was assessed using food frequency questionnaires. There was no change in carotenoid intake during the trial. Responders had a lower intake of dietary fiber, fruits, folate, and vitamin E supplements than did nonresponders. In conclusion, the activity of **beta-carotene** in patients with oral **leukoplakia** was confirmed. The responses produced were durable for 1 year.

Known Hazards: Use of **beta-carotene** has been associated with an increased risk of lung cancer in people who smoke or who have been exposed to asbestos. One study of 29,000 male smokers found an 18% increase in lung cancer in the group receiving 20 mg of **beta-carotene** a day for 5 to 8 years. Another study of 18,000 people found 28% more lung cancers in people with a history of smoking and/or asbestos exposure. These people took 30 mg of **beta-carotene** in addition to 25,000 Units of retinol (a form of vitamin A) a day for 4 years. However, one study of 22,000 male physicians, some of them smokers or former smokers, found no increase in lung cancer. These people took 50 mg of **beta-carotene** every other day for 12 years. If you smoke or have a history of smoking or asbestos exposure, you should not take large amounts of **beta-carotene** supplements for long periods of time. However, foods that are rich in **beta-carotene** are considered safe and appear to lower the risk of some types of cancer and possibly heart disease.

The results from the ATBC Study and the **Beta-Carotene** and Retinol Efficacy Trial (CARET) suggest that smokers should avoid taking **beta-carotene** supplements. The best advice for smokers who want to reduce their risk of lung cancer and many other cancers is still the most direct: Stop smoking.

Yellowing of palms, hands, or soles of feet, and to a lesser extent the face (this may be a sign that your dose of **beta-carotene** as a nutritional supplement is too high).

- U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894. **Beta-Carotene** (Systemic)
- U.S. Department of Agriculture Agricultural Research Service. - Carotenoids Show Their True Colors - **Beta Carotene** Boosts Immunity in Elders
- Garewal HS; Katz RV; Et al. **Beta-carotene** produces sustained remissions in patients with oral **leukoplakia**: results of a multicenter prospective trial. Arch Otolaryngol Head Neck Surg 1999 Dec;125(12):1305-10